AMERICAN

Journal of Pharmacy

AND THE SCIENCES SUPPORTING PUBLIC HEALTH

Pharmacy Week Window in Philadelphia National Bank
Arranged by Joint Cooperation of the Philadelphia
National Bank; Smith, Kline and French
Laboratories, and the Two Colleges
of Pharmacy in Philadelphia.

Since 1825 *October 1957*

American Journal of Pharmacy

Published monthly by the Philadelphia College of Pharmacy and Science
43d Street, Kingsessing and Woodland Avenues, Philadelphia 4, Pa.

Annual Subscription $4.00 — Foreign Postage, 25 Cents Extra
Single Numbers, 40 Cents — Back Numbers, 50 Cents

Entered as Second-Class Matter March 27, 1937, at the Post Office at Philadelphia, Pa.
Under Act of March 3, 1879

A NEW NON-NARCOTIC ANALGESIC
WITH THE POTENCY OF CODEINE

DARVON

(Dextro Propoxyphene Hydrochloride, Lilly)

is the new, chemically different analgesic which is equally as potent as codeine yet much better tolerated. Orally effective, 'Darvon' is valuable in any disease associated with pain. It does not come within the restrictions of the Harrison Narcotic Act.

'Darvon' is available in 32 and 65-mg. pulvules.

DARVON COMPOUND

(Dextro Propoxyphene and Acetylsalicylic Acid Compound, Lilly)

further increases effectiveness by combining the analgesic action of 'Darvon' with the antipyretic and anti-inflammatory benefits of 'A.S.A. Compound.'*

Each Pulvule 'Darvon Compound' provides:

'Darvon'	32	mg.
Acetophenetidin	162	mg.
'A.S.A.' (Acetylsalicylic Acid, Lilly)	227	mg.
Caffeine	32.4	mg.

An intensive detailing, direct mail, and journal advertising program is certain to create a heavy demand for these important products. Order adequate stocks from your Lilly wholesale distributor. Supplied in bottles of 100.

*'A.S.A. Compound' (Acetylsalicylic Acid and Acetophenetidin Compound, Lilly)

Lilly
QUALITY / RESEARCH / INTEGRITY

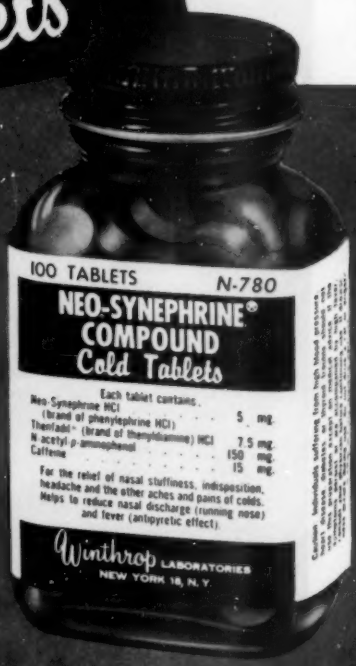
ELI LILLY AND COMPANY, INDIANAPOLIS 6, INDIANA, U. S. A.

720727

New!

NEO-SYNEPHRINE® COMPOUND Cold Tablets

MORE COMPLETE CONTROL of common cold syndrome



This orally effective decongestant, analgesic, antipyretic and antihistaminic tablet is a new addition to the famous Neo-Synephrine line which will be intensively promoted to physicians in your area.

Order Today!
Be prepared for the coming "COLD" season

BOTTLES OF 100 TABLETS

NEO-SYNEPHRINE
COMPOUND
Cold Tablets

Winthrop LABORATORIES
1450 Broadway, New York 18, N. Y.
PHARMACEUTICALS IN DAILY DEMAND
ETHICALLY ADVERTISED AND DETAILED

Neo-Synephrine (brand of phenylephrine) and Thenfadil (brand of thenyldiamine), trademarks reg. U.S. Pat. Off.

AMERICAN JOURNAL OF PHARMACY

AND THE SCIENCES SUPPORTING PUBLIC HEALTH

Since 1825

Vol. 129 OCTOBER 1957 No. 10

CONTENTS

Editorial

An Imminent Threat 348

Articles

Testing for Sterility of Corn Oil. Part III. The Use of Non-ionic Surfactants. By K. E. Avis and L. Gershenfeld 350

The Formulation of an Antihistamine Elixir. By M. Barr and L. F. Tice 358

Studies of the Genus Thymus. Part I. By I. Hassan and M. S. Dunn 362

Drug Information Sources (India and Japan) 372

Selected Abstracts 378

E D I T O R I A L

AN IMMINENT THREAT

SLOWLY but surely, those who believe in socialized medicine are bringing it into being by piecemeal legislation rather than by a frontal attack on the free enterprise system. Already, vast numbers of our citizens are eligible for "free" medical care provided for by federal or state taxes levied against everyone. Each new group added to the number already covered by some government plan may by itself seem insignificant but the total continues to grow not only in terms of numbers but in the per cent of our population which is involved.

A new bill introduced in the closing days of the last session of Congress (H. R. 9467) is the latest attempt to bring about socialized medicine by back door maneuvers. Already, it has the support of many of our "liberals" including the AFL-CIO, and others who look to government medicine as the ideal toward which we all should strive. The bill would underwrite all medical expenses for persons receiving old-age or survivor's benefits under our present Social Security plan. It would cover semi-private hospital care for up to sixty days each year as well as a similar period of nursing-home care. Payment would also be made for all medical and surgical services.

As might be expected, Social Security taxes would be greatly increased for both employer and employee and the plan would be administered by the government with every aspect of medical care regulated by the government. In describing this bill, its sponsor, Representative Aime Forand, stated that

> "There shall be no government control of either the practice of medicine or the administration or operation of hospitals and nursing homes. Each agreement with a hospital . . . shall be made upon such . . . terms and conditions as are consistent with the efficient and economical administration of this section (of the bill) . . ."

Can anyone reading this believe that the federal government would not lay down the terms which it believes constitute efficient and economic administration? The Secretary of HEW would also be

empowered to enter into agreements with those rendering surgical and other services including the rates of payment.

Thus does the Forand Bill attempt to cover a huge number of our older citizens by an all-inclusive national health plan. With part of our citizens so covered, it would be a relatively easy matter to include still more. Already, we have medical and surgical benefits for veterans, the dependents of all those in the military services, and —in most states—the medically indigent.

Those in the health professions should take the time to study what has happened in those countries where a national health plan has been adopted. Instead of physicians, pharmacists, dentists, and similar practitioners being free and independent, they are little more than employees of the state. So difficult has been the relationship between the government and physicians in England that even a general strike of physicians has been seriously considered.

While, at the moment, we have a conservative influence in the executive branch of our government, this cannot be counted on as a permanent force and it would be well for our professions—if they cherish their independence of thought and action—to prepare for a long and bitter struggle.

Those who champion state medicine do so in good faith because they do not comprehend or appreciate the meaning of personal freedom and liberty. They are so imbued with the philosophy of security that they are willing to pay any price for it. Throughout the history of man, this is the way that liberty has been lost and people finally enslaved. Here in the United States, we are well on our way down this same path. For a brief period of a few years, conservative influences have "held the dike" but, to those who will take time to reflect on the likely future, it seems bleak indeed. Our opponents are not complacent about things and, if our philosophy is to prevail, we cannot afford to be.

L. F. Tice

TESTING FOR STERILITY OF CORN OIL

Part III

The Use of Non-ionic Surfactants *

By Kenneth E. Avis ** and Louis Gershenfeld ***

Introduction

THE survey of American manufacturers of parenteral products, referred to in the Preface to Part I (1) of this series of studies, revealed that nearly one-half of the manufacturers who responded that they used the U. S. P. sterility testing method for determining the sterility of oleaginous preparations were not satisfied with the method. Such comment provides a challenge for investigating techniques which may give results more satisfactory than those obtained with the present U. S. P. method. Although the Millipore filtration technique described in Part II (2) of this series of studies appears to provide an improved method for the recovery of spores from a liquid oleaginous solution, a filtration procedure is subject to a greater risk of inadvertent contamination than are culture tube inoculation methods. Therefore, a study of several culture tube inoculation procedures was undertaken, the results from which are presented here.

The literature findings, summarized in the Preface to Part I (1), revealed that the results from only a few studies on the sterility testing of oils had been reported. In one instance, an emulsification technique for the sterility testing of liquid petrolatum was employed (3). By the technique reported, an inoculum of the oil was emulsified and then an inoculum of the emulsion was transplanted to nutrient broth and incubated, as in Method C reported herein. The same author also

---

* Presented at the 104th meeting of the American Pharmaceutical Association, Scientific Section, May 1, 1957, New York City.

** Associate Professor in Pharmacy, Philadelphia College of Pharmacy and Science.

*** Professor of Bacteriology and Director of the Bacteriology Department, Philadelphia College of Pharmacy and Science.

reported a method in which liquid petrolatum was dispersed in polyethylene glycol. An inoculum of this dispersion was centrifuged in nutrient broth and then incubated, as in Method D reported herein. The author reported that growth was obtained in a high proportion of the tests with both methods. However, it should be noted that a heavy suspension of bacteria was used.

Methods

In all of these experiments, corn oil was used exclusively as the oil to be tested. Although it was recognized that other oils might have somewhat different effects in the methods studied, the scope of the over-all problem did not permit investigation of other oils. Likewise, only the spores of *Bacillus cereus* ATCC No. 7064 were used in these experiments. It is recognized that other organisms may have reacted differently in some respects if employed in the methods herein reported.

In all of these experiments, the spores were dispersed in a dry state in sterile corn oil or sterile saline by milling as described in Part I (1) of this series of studies.

Method A

Throughout the investigation, the U. S. P. sterility test procedure was used as the method of comparison for the procedures studied. However, it should be noted that the method as used was a slight modification of the U. S. P. sterility testing procedure for oils.

An inoculum of the corn oil spore suspension was introduced into 10 ml. of trypticase soy broth (TSB) or fluid thioglycollate medium (FTM) in 19 x 150 mm. culture tubes. The volume of inoculum varied from 0.01 ml. to 5 ml. A volume of 0.1 ml. was most frequently used. When 1 ml. or more was used and a layer of oil sealed off the medium in the tube, growth was not always obtained, even from heavily contaminated inocula. The inoculum was distributed through the medium with vigorous shaking by hand. The tubes were also shaken frequently by hand during the incubation period of at least 7 days at 30 to 32° C. One 5 mm. glass bead was introduced into the tubes of TSB to aid in the dispersion of the oil inoculum. It was observed that the test organism grew more quickly in TSB than in FTM. Consequently, TSB was used most frequently in the tests with each of the methods, although FTM was employed at occasions throughout the study.

Method B

This method varied from the U. S. P. procedure in that the non-ionic surfactant Tween 80[a] was employed as a solubilizer or dispersant of small globules of the corn oil samples in the culture media, since Tween 80 is miscible with both fixed oils and aqueous solutions. It was found that 1 ml. of Tween 80 provided a clear solution when mixed with about 20 or more ml. of corn oil. Thus, a test method was developed which differed from the U. S. P. procedure only in that 1 ml. of Tween 80, sterilized in a hot air oven at 140° C. for 4 hours, was mixed with about 20 or more ml. of the spore suspension in corn oil before an inoculum was transferred to culture medium. The size of inoculum, volume of culture medium, shaking procedure and incubation were as for Method A.

It was observed that FTM and TSB became turbid upon inoculation when Tween 80 was present in the inoculum. Since this turbidity was less pronounced with TSB, the latter was used most frequently in these studies.

Method C

This method was similar to the emulsification method described by another author (3). An inoculum of a spore suspension in corn oil, usually 1 ml., was coarsely emulsified by shaking and stirring with a sterile pipette in 10 ml. of a sterile aqueous mixture of non-ionic surfactants containing 0.2 per cent Tween 80 and 0.3 per cent G-2800[b] (T-G). At times, one-half this concentration was used. In several trials, 0.25 to 1 per cent Triton X-100[c] (TrX), also a non-ionic surfactant, was employed for emulsification and, in a few instances, 0.2 per cent Tween 80 was used. Each of the surfactant solutions were sterilized by autoclaving at 121° C. for 20 minutes. Triton X-100 provided somewhat better emulsification than the other agents, based upon macroscopic observation. An inoculum of 1 ml. of the emulsified material was then dispersed in TSB or FTM. Both media became turbid upon the introduction of the inocula and, unless growth was quite pronounced, transplanting was necessary to check for the presence or absence of growth.

[a] Polyoxyethylene sorbitan mono-oleate. Supplied by Atlas Powder Co., Wilmington, Del.

[b] Polyoxypropylene mannitol dioleate. Supplied by Atlas Powder Co., Wilmington, Del.

[c] An alkyl aryl polyether alcohol. Supplied by Rohm and Haas, Phila., Pa.

Method D

A volume of 6 ml. of spore suspension in corn oil was dispersed in an equal volume of polyethylene glycol 400, previously sterilized in a hot air oven at 140° C. for 4 hours. This mixture was then centrifuged at 1500 to 2000 r.p.m. for 1 hour in sterile centrifuge tubes. A sterile pipette was introduced through the oil layer and a 1 ml. inoculum removed from the bottom (tip) of the tube. This was similar to the procedure described by another author (3). Employing a modification of this technique, the tube and its contents were shaken vigorously after centrifuging, the oil allowed to rise, and then an inoculum of the polyethylene glycol layer was removed by introducing a sterile pipette through the oil layer. These inocula were then dispersed by shaking in TSB or FTM. The purpose of centrifuging was to try to aid in the transfer of the test spores from the supernatant layer to the polyethylene glycol layer.

Method E

This method differed from Method C only in that the emulsified inoculum was centrifuged in TSB at 1500 to 2000 r.p.m. for 1 hour. The tubes were then incubated with or without frequent shaking during the incubation period.

In methods A through E, the incubation period was not less than 7 days at a temperature of 30 to 32° C. In all cases, 10 ml. of TSB or FTM were used in 19 x 150 mm. culture tubes. Shaking was performed by hand.

Findings

A total of 1008 tests were performed to detect the presence of spores of *B. cereus* in samples of corn oil by means of the five culture tube methods. Of these tests, 532 were conducted by means of Method A and 413 by means of Method B. The results from all of these test procedures are recorded in Table I.

TABLE I

RECOVERY OF B. CEREUS SPORES FROM CORN OIL
CULTURE TUBE METHODS

No. of Spores[a] Per Inoculum[b] of Corn Oil	Method A[c] No. of Tubes Showing		Method B[d] No of Tubes Showing		Method C[e] No. of Tubes Showing		Method D[f] No. of Tubes Showing		Method E[g] No. of Tubes Showing	
	G[h]	NG[i]	G	NG	G	NG	G	NG	G	NG
less than 1	2	67	3	33	—[j]	—	—	—	1	1
1-2.5	13	185	14	160	0	2	1	0	0	2
3-7.5	3	20	—	—	0	2	4	2	0	4
10-15	14	117	60	107	0	7	0	3	0	2
18-25	7	8	5	2	0	5	—	—	0	1
30-40	12	5	—	—	—	—	0	1	0	1
50-100	21	11	16	0	0	4	1	1	2	1
150-500	17	5	7	0	—	—	0	4	1	1
600-1,000	9	1	4	0	1	1	4	0	0	2
1,500-10,000	7	0	2	0	—	—	0	1	—	—
above 10,000	8	0	—	—	—	—	—	—	—	—
Total Tests	113	419	111	302	1	21	10	12	4	15

[a] Based upon the count of the number of *B. cereus* spores in the suspension dried in test tubes. These were dispersed in the corn oil samples.

[b] Volume of inocula varied from 0.01 to 5 ml. In most cases, it was 0.1 ml.

[c] Method A—Inoculum shaken by hand frequently during incubation in 10 ml. of TSB or FTM in test tubes (19 x 150 mm.).

[d] Method B—Same as A except that sterile Tween 80 was mixed with corn oil sample, usually 1 part Tween 80 to 20 or more parts corn oil, before inocula were transferred to TSB or FTM.

[e] Method C—Inoculum emulsified in 10 ml. of a sterile mixture of 0.2% Tween 80 and 0.3% G-2800, or 0.2% Tween 80, or 1% Triton X-100, then inoculum of emulsified material dispersed in TSB or FTM.

[f] Method D—Inoculum centrifuged in 6 ml. of sterile polyethylene glycol 400 at 1,500 to 2,000 r.p.m. for 1 hour, then inoculum dispersed in TSB or FTM.

[g] Method E—Same as C except emulsified inoculum centrifuged in TSB at 1,500 to 2,000 r.p.m. for 1 hour before incubation.

[h] G = Growth.

[i] NG = No Growth.

[j] — = No data.

The theoretical number of spores, as used herein, is the number of spores which were present in the volume of standardized spore suspension dried in the tube, the latter being used for the preparation, by milling, of the spore dispersion in the corn oil or in the saline. As

reported in Part I of this series, the spore count from inocula in trypticase soy agar (TSA) plates was only from about ⅓ to ½ as high when the spores had been dispersed in corn oil as when in saline. It was also observed that the spore recovery in TSA from saline dispersions was sometimes only ⅓ to ½ as high as the theoretical number of spores present. Thus, for example, it was frequently the case that an average of about 2 spores would be recovered in TSA from a corn oil spore suspension containing a theoretical number of 10 spores. In view of this observation, in the series reported (See Table I, Methods A and B), more tests were conducted using 15 or less spores per inoculum of corn oil.

It will be noted from the data in Table I that in the tests in which a theoretical number of 25 or less spores were present in each inoculum of corn oil tested by Method A, positive findings were obtained in less than 50 per cent of the tests. When the theoretical number of spores was 30 or higher, positive findings exceeded 75 per cent of the tests. Positive findings in 100 per cent of the tests was approached when the theoretical count was over 1000 spores per inoculum. On the other hand, positive findings in 100 per cent of the tests was approached using Method B when the theoretical count was 50 or more spores per inoculum.

When the theoretical number of spores was from 10 to 15 in each inoculum, only 14 of 131 tests showed growth (10.7 per cent) using Method A as the testing procedure. On the other hand, when Method B was used at this same spore concentration, 60 of 167 tests showed growth (36 per cent). Based on the theoretical range of from 1 to 15 spores (probably a recoverable number of 3 or less spores) per inoculum of corn oil, 30 of 352 tests (8.5 per cent) showed growth when tested by Method A while 74 of 341 (21.7 per cent) showed growth by Method B. Since it is not likely that an oleaginous preparation intended for injection would have a heavy concentration of contaminating microorganisms, the lower concentrations of spores in this study are of greatest interest with regard to the sterility test findings. Therefore, based upon these studies, it would appear that Method B is 2 to 3 times more effective than Method A as a procedure for the recovery of spores of *B. cereus* from corn oil in the theoretical spore density range of 15 or less per inoculum. However, neither method approaches 100 per cent recovery of the theoretical number of spores present.

As may be seen from the data recorded in Table I, Methods C, D, and E did not give satisfactory and consistent recovery of spores from corn oil. It is particularly to be noted that even when large numbers of spores were present in each inoculum of the corn oil suspension, some of the findings were negative. Therefore, these procedures were not studied extensively.

Summary and Conclusions

Five culture tube inoculation methods were studied for their effectiveness in the recovery of spores of *B. cereus* from corn oil. Altogether, 1008 tests were performed. Varying spore densities were employed with each method.

In Method A, an inoculum of the corn oil suspension in 10 ml. of TSB or FTM was shaken in the presence of a 5 or 6 mm. glass bead. During at least 7 days incubation at 30 to 32° C., further shaking was given at frequent intervals. This was a slight modification of the U. S. P. sterility testing procedure for oils.

Method B differed from Method A in that 1 part of sterile Tween 80 was mixed with 20 or more parts of the corn oil suspension before inocula were transferred to TSB or FTM.

Method C consisted of emulsifying an inoculum of the corn oil suspension in 10 ml. of a sterile mixture of 0.2 per cent Tween 80 and 0.3 per cent of G-2800, or 0.2 per cent Tween 80, or 1 per cent Triton X-100. An inoculum of the emulsified material was then dispersed in 10 ml. of TSB or FTM and incubated at 30 to 32° C.

Method D consisted of dispersing and then centrifuging 6 ml. of corn oil suspension in 6 ml. of sterile polyethylene glycol 400, at a speed of 1500 to 2000 r.p.m. for 1 hour. An inoculum from the polyethylene glycol layer was then dispersed in TSB or FTM and incubated as above.

Method E differed from Method C only in that the emulsified inoculum in TSB or FTM was centrifuged at 1500 to 2000 r.p.m. for 1 hour before incubation.

The recovery of spores from corn oil suspensions having a range of spore densities using Methods C, D, and E was found to be inconsistent and, relatively few positive findings were obtained from known positive suspensions. Therefore, studies with these methods were not continued beyond a small number of tests. However, Method B, employing a non-ionic surfactant in the oil as a dispersant, was

found to be 2 to 3 times more efficient than Method A (U. S. P. procedure, slightly modified) in the recovery of spores of *B. cereus* from corn oil suspensions. This more effective recovery of spores was noted at low as well as high spore densities. Therefore, this method warrants further study as an improved sterility testing procedure for oils.

BIBLIOGRAPHY

(1) Avis, K. E., and Gershenfeld, L., "Testing for sterility of corn oil. Part I. Dispersion of spores in corn oil and in saline". *Am. Ju. Pharm 129:*234 (1957).

(2) Avis, K. E., and Gershenfeld, L., "Testing for sterility of corn oil. Part II. The use of filters and filtration procedures". *Am. J. Pharm. 129:*290 (1957).

(3) Pollack, R. L., "Isolation of bacteria from liquid petrolatum". Unpublished Bachelor of Science thesis, Department of Bacteriology, Philadelphia College of Pharmacy and Science, 1949.

THE FORMULATION OF AN ANTIHISTAMINE ELIXIR *

By Martin Barr and Linwood F. Tice

THE widespread use of antihistamine therapy in children as well as adults makes an elixir of such drugs an important dosage form. In the formulation of such elixirs, the selection of a suitable vehicle and one having maximum taste appeal is important. Such elixirs should not have too high an alcohol content and the use of some polyol for its sweetening and bodying effect is better than the use of syrup.

In this study, chlorpheniramine maleate was selected as the antihistamine since it is highly favored by many pediatricians. Using this official drug, an elixir formula was developed having good stability, low alcohol content, and excellent taste appeal based on panel studies. Glycerin and Sorbitol in the form of Sorbitol Solution, N. F. were the polyols studied for their relative merit, the poor flavor of propylene glycol being well known.

Experimental Procedure

Chlorpheniramine maleate is soluble, 1 in 4 in water and 1 in 10 in alcohol. Since it was evident that no solubility problem existed in formulating the elixir, the major problem in the developmental work consisted of selecting the ideal vehicle for the drug.

Alcohol was selected as an ingredient of the vehicle since a hydroalcoholic solvent is the principal characteristic of an elixir. It is also one of the most acceptable and least toxic preservatives. Sorbitol Solution, N. F. X [1] and glycerin were both compared as the ingredient to serve as a sweetening and bodying agent. Several flavoring agents were studied for their effectiveness in masking the taste of chlorpheniramine maleate. It was found that a combination of 0.01% benzaldehyde [2] and 0.02% vanillin [3] provided an excellent flavor. It was, therefore, decided to use this combination throughout the study.

---

* From the Department of Pharmacy, Philadelphia College of Pharmacy and Science. Work supported by a research grant from the Atlas Powder Company, Wilmington, Delaware.

1. Sorbo®, Atlas Powder Company, Wilmington, Del.
2. Benzaldehyde, N. F. X, Merck & Co., Inc., Rahway, N. J.
3. Vanillin, U. S. P. XV, Mallinckrodt Chemical Works, St. Louis, Mo.

Development of Vehicle

Elixirs containing 2 mg. of chlorpheniramine maleate [4] in 5 ml. (0.04%) [5] of elixir were prepared in which the concentrations of alcohol and polyol were varied. Numerous combinations were prepared in which the alcohol content ranged from 10 to 20% and the polyol content from 25 to 65%. As previously stated, a combination of 0.01% benzaldehyde and 0.02% vanillin was selected as the flavoring agent. The elixirs were colored by the use of 0.1% Amaranth Solution, U. S. P. XV.

Final Formula

It was found that a combination of 10% alcohol and 45% Sorbitol Solution in the vehicle was the most satisfactory. Such a formulation, when flavored with 0.01% benzaldehyde and 0.02% vanillin and colored with 0.1% Amaranth Solution, has remained stable for one year at 25° C. and 4° C. It does not require filtration except for lint, dirt particles, etc.

The recommended formula for Chlorpheniramine Elixir and the directions for its preparation follow:

Chlorpheniramine Maleate	0.4 Gm.
Benzaldehyde	0.1 ml.
Vanillin	0.2 Gm.
Amaranth Solution	1. ml.
Alcohol	100. ml.
Sorbitol Solution	450. ml.
Purified Water q.s. ad	1000. ml.

Dissolve the chlorpheniramine maleate in 400 ml. of purified water. Add successively the benzaldehyde and vanillin—previously dissolved in the alcohol, Sorbitol Solution, Amaranth Solution, and enough purified water to make 1000 ml. Mix well and filter, if necessary.

The finished elixir is pink in color, has a most pleasing taste, and a pH of 5.3-5.5.

---

4. The authors gratefully acknowledge the cooperation of Schering Corporation, Bloomfield, N. J. in supplying the chlorpheniramine maleate which is patented by them as Chlortrimeton maleate.

5. Although the usual dose of chlorpheniramine maleate is 4 mg., doses of 2 mg. are common, especially for children. Therefore, the elixirs were prepared to contain 2 mg. of drug per 5 ml. dose of elixir.

Bacteriological testing indicated that no additional preservative other than the alcohol present is needed in the elixir since the product when inoculated with bacteria and molds did not support growth.

Taste Panel Testing

In order to determine whether Sorbitol Solution or glycerin was superior as a sweetening agent in the newly formulated elixir, a taste panel, consisting of thirty students, was used. Preference was determined for an elixir containing 45% Sorbitol Solution, or one of two other elixirs in which glycerin replaced the Sorbitol Solution on an equal volume or equal weight basis. One elixir, in which glycerin replaced the Sorbitol Solution on an equal volume basis, contained 45% v/v glycerin. The other elixir, in which glycerin replaced Sorbitol Solution on an equal weight basis, contained 32.90% v/v glycerin.[6]

The members of the taste panel were asked to express their opinions of the tastes of the three elixirs by the use of the following ratings: "no difference", "slightly superior", "moderately superior", and "strongly superior". The panel was divided so that the effect of order of tasting samples was removed.

The conclusions reached based on the panel results were that the elixir containing 45% v/v Sorbitol Solution was definitely superior to the elixir containing 32.90% v/v glycerin. The panel assigned a "moderately superior" rating to it. In this test, the polyols were evaluated on an equal weight basis.

The panel also judged the elixir containing 45% v/v Sorbitol Solution definitely superior to the elixir containing 45% v/v glycerin. The panel assigned a "moderately superior" rating to it but it was closer to a "strongly superior" rating than in the previous test. In this study, the polyols were evaluated on an equal volume basis.

Discussion

In the formulation of a chlorpheniramine maleate elixir, Sorbitol Solution, N. F. X was found ideally suited as a bodying and sweetening agent.

---

6. 32.90% v/v glycerin is equivalent to 41.18% w/v glycerin. 45% v/v Sorbitol Solution is equivalent to 41.18% w/v D-sorbitol. Sorbitol Solution contains 91.50% w/v D-sorbitol. Anhydrous glycerin (Shell Chemical Co.) was used in this study.

It was found that an antihistamine elixir was superior in taste when it contained 45% v/v Sorbitol Solution as compared with one containing glycerin on either an equal volume or equal weight basis. The results seem to indicate the superiority of Sorbitol Solution as compared with glycerin as a sweetener and bodying agent in pharmaceuticals. In this study, a direct comparison of the sweetening effect of Sorbitol Solution and glycerin was possible since no extremely unpleasant drugs such as barbiturates were present. Such drugs often make comparative taste studies on sweetness very difficult, if not impossible. Although glycerin has good sweetening properties, it imparts an acrid taste which is not pleasant. Sorbitol is devoid of this acrid taste.

Sorbitol Solution is also superior to syrup as a sweetener in this type of elixir since sucrose in time undergoes inversion resulting in a change of color, taste, and consistency of the product.

Summary

1. A formula for an elixir containing chlorpheniramine maleate has been developed.

2. Sorbitol Solution, N. F. X, is utilized in the elixir as a sweetening and bodying agent in a concentration of 45% v/v.

3. The elixir is very pleasing to the taste, has a pH of 5.3-5.5, is pink in color, and does not support the growth of microorganisms.

4. Evidence has been obtained pointing to the superiority of Sorbitol Solution, N. F. X, as compared with glycerin as a sweetening agent in products of this type.

REFERENCES

(1) "The United States Pharmacopeia", Fifteenth Rev., Mack Printing Co., Easton, Pa., pp. 151-152.

STUDIES OF THE GENUS THYMUS

Part I

Comparison of the Diagnostic Microscopical Characteristics of Thymus vulgaris Linn. and Thymus Serpyllum Linn.

By Ikram Hassan * and Marin S. Dunn **

FOR sometime, the authors have been interested in microscopical studies of various species of the Genus Thymus. In this paper is a report of our findings in the cases of Thymus vulgaris Linn. and Thymus Serpyllum Linn., tissue elements of which were studied from the leaves and flowering tops.

Three samples of Thymus vulgaris (commercial material from S. B. Penick and The Meer Corporation and an herbarium sheet from the Martindale Collection of the Philadelphia College of Pharmacy and Science) and seven samples of Thymus Serpyllum, labelled as follows were used:

1. Thymus Serpyllum		Meer Corporation.
2. Thymus Serpyllum		S. B. Penick.
3. Thymus Serpyllum	Linn.	Martindale Collection.
4. Thymus Serpyllum	var. albus (flowering)	Cloud Hill Nurseries of Quakertown, Pa.
5. Thymus Serpyllum	var. coccineus (flowering)	
6. Thymus Serpyllum	var. citriodorous	Tyler Arboretum.
7. Thymus Serpyllum		Drug Plant Laboratory University of Washington Seattle, Washington.

The identification of the material used in these studies, even though obtained from reputable sources was verified in three ways:

1. The commercial samples from S. B. Penick and Meer Corporation which were received as broken plant material were micro-

* Instructor, Department of Biology, Philadelphia College of Pharmacy and Science, Philadelphia, Pa. In partial fulfillment of the requirements for the Degree of Doctor of Science.

** Professor of Biology and Director of the Biology Laboratories, Philadelphia College of Pharmacy and Science, Philadelphia, Pa.

scopically examined in powdered state and checked with the elements mentioned in Youngken (2).

2. The plants which were received entire, but without flowers, i.e. from the Tyler Aboretum and the Drug Plant Laboratory, University of Washington, Seattle, Washington, were similarly ground up and the microscopical characters examined as mentioned above.

3. The morphological characteristics of those plants received in the flowering condition were checked with the descriptions of Bailey (3), Hegi (4), Wittmack (5), Grieve (6), Youngken (2), and Rhode (7).

Method of Study

As a preliminary, a commercial sample of Thymus vulgaris was taken and small pieces of upper and lower leaf epidermis and stem epidermis were scraped away and thus isolated. These pieces were placed on slides in such a way that the outer surface of the stem epidermis, the upper surface of the upper leaf epidermis and the lower (outer) surface of the lower leaf epidermis were uppermost (nearest to the eye), and cleared in chloral sol. (50 gms. in 20 cc. of water). A calyx tube was split and half of the tube was mounted with outer epidermis uppermost and the other half with inner epidermis uppermost on different slides in chloral solution. All these slides were very slightly warmed to hasten the clearing process. The various histological elements found on these slides were examined first under low power (100x) and then under high power (430x).

In a similar way, studies were carried out on material obtained from the herbarium sheet. A leaf, a small piece of stem, and a flower were detached from the herbarium sheet and studied as in case of the commercial material.

After the "get-acquainted" study of these elements, the samples of Thymus vulgaris from the sources mentioned above, were powdered separately by suspending in carbon tetrachloride and subjecting them to the action of the wet grinding mill. The powders were then individually defatted, cleared, and stained with Bismark Brown as given in the method of Silverman and Dunn (1). These powders were examined under the microscope, and camera-lucida drawings were made (Figs. 4, 5).

In exactly the same way, the studies were carried out on material labelled as Thymus Serpyllum and var. albus and var. coccineus.

Histological Observations

The following tabulated data will be helpful in making comparison, as will reference to figures 1, 2, 3, 4, and 5. The measurements in microns given in the table are not to be construed as absolute and only represent the averages of a few determinations each and as such are given only to furnish general guides to size. Scars have been emphasized in drawings.

TABLE

Plant part examined	Thymus vulgaris	Thymus Serpyllum, particularly var. albus and var. coccineus
Leaf	1. *Upper Epidermis:* walls beaded in appearance, cuticle striated, stomata not many, abundant hairs present as shown below.	1. *Upper Epidermis:* walls beaded in appearance, cuticle striated, stomata not abundant, hairs present as shown below.
	2. *Trichomes:*	2. *Trichomes:*
	A. *Nonglandular hairs.* All nonglandular trichomes on leaf have papillose walls. The following different kinds were noticed:	A. *Nonglandular hairs.* Papillose walls. The following different kinds of hairs were noticed:
	a. Papilla-like, about 35 μ long.	a. Papilla-like, up to 20 μ long.
	b. 2-5 celled up to 250 μ long.	b. 2-6 celled up to 800 μ long, only in varieties albus and coccineus, found near the margin of the leaves.
	c. 1-2 celled, sharply pointed straight or curved up to 100 μ long.	c. 1-2 celled sharply pointed straight or curved up to 150 μ long found in varieties albus and coccineus.
	B. *Glandular hairs.*	B. *Glandular hairs.*
	a. Multicellular, 8-12 celled head, with or without a stalk.	a. Multicellular, 8-12 celled head, with or without a stalk.
	b. 2-3 celled i.e. 1 celled head and stalk; 1 celled head and 1-2 celled stalk.	b. 2 celled i.e. 1 celled head and 1 celled stalk.
	3. *Trichome Scars:* numerous in powdered drug.	3. *Trichome Scars:* rare, when present noticeably small in diameter.
	4. *Lower Epidermis:* Walls beaded, trichomes as in upper epidermis, stomata present, walls wavy, cuticle faintly striated.	4. *Lower Epidermis:* Walls slightly beaded, cuticle not striated, trichomes as in upper epidermis, nonglandular trichomes rare, stomata in abundance.
Stem	1. *Epidermis:* Walls slightly beaded, cuticle not striated.	1. *Epidermis:* Slightly beaded, cuticle striated.
	2. *Trichomes:*	2. *Trichomes:*
	A. *Nonglandular hairs:* mostly near the nodal region.	A. *Nonglandular hairs:* very rare in Thymus Serpyllum, when present.

Plant part examined	Thymus vulgaris	Thymus Serpyllum, particularly var. albus and var. coccineus
	a. Papilla-like, not very common.	a. Papilla-like, up to 25 μ long.
	b. 2-3 celled, sharply pointed, straight or curved, up to 150 μ; walls papillose.	b. 2-3 celled up to 120 μ, papillose walls, sharply pointed, straight or curved. Specimens labelled var. albus and var. coccineus showed more hairs than those in material simply labelled Thymus Serpyllum. c. In coccineus 2-5 celled, up to 350 μ, papillose walls.
	B. *Glandular hairs:*	B. *Glandular hairs:*
	a. Multicellular glandular hairs similar to those found on the leaf rarely present.	a. Multicellular glandular hairs similar to those found on the leaf, rare.
	3. *Trichome Scars:* Numerous.	3. *Trichome Scars:* Rare in material labelled Thymus Serpyllum, but in var. albus and var. coccineus more scars, although fewer than in Thymus vulgaris.
Calyx	1. *Outer Epidermis:* Hairy all-over, walls not beaded, cuticle striated. The following types of trichomes were found:—	1. *Outer Epidermis:* Almost glabrous, walls slightly beaded, cuticle striated. In var. albus and var. coccineus, trichomes were found as follows:—
	2. *Trichomes:*	2. *Trichomes:*
	A. *Nonglandular hairs.*	A. *Nonglandular hairs.*
	a. 1-celled, papilla-like with papillose surface or long, pointed, hooked or straight up to 50 μ long.	a. 1-celled, papilla-like with papillose surface or longer up to 100 μ.
	b. 2-5 celled, papillose surface up to 250 μ long.	b. 2-5 celled, not very common.
	B. *Glandular Trichomes.*	B. *Glandular Trichomes.*
	a. 2-3 celled i.e. 1 celled head and stalk; 1 celled head and 1-2 celled stalk.	a. 2 celled usually, with 1-celled head and stalk.
	b. 8-12 celled head; stalk 1 celled or no stalk.	b. 8-12 celled head, stalk 1 celled or no stalk.
	3. *Trichome Scars:* Numerous.	3. *Trichome Scars:* Rare in material marked Thymus Serpyllum, but in var. albus and var. coccineus more scars, although fewer than in Thymus Vulgaris.
	4. *Inner Epidermis:* Surface similar to outer epidermis but long trichomes present only at the throat of calyx. These trichomes are up to 7 cells long, with papillose surface, up to 700 μ long.	4. *Inner Epidermis:* Surface similar to outer epidermis, but long trichomes present only at the throat of calyx. These trichomes are up to 7 cells long, with papillose surface, up to 750 μ long.

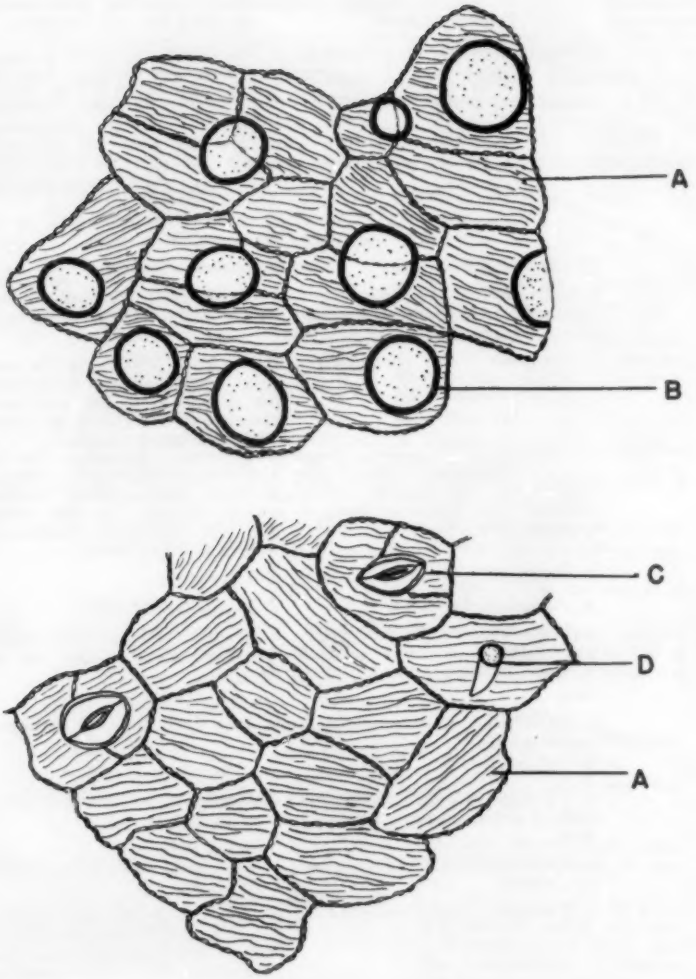


FIG. 1—EPIDERMIS OF LEAF × 340.

(Top) Thymus Vulgaris. (Bottom) Thymus Serpyllum.
A—Epidermal Striation. B—Trichome Scar. C—Stomata.
D—1-Celled Non-Glandular Trichome. (Scars Emphasized.)

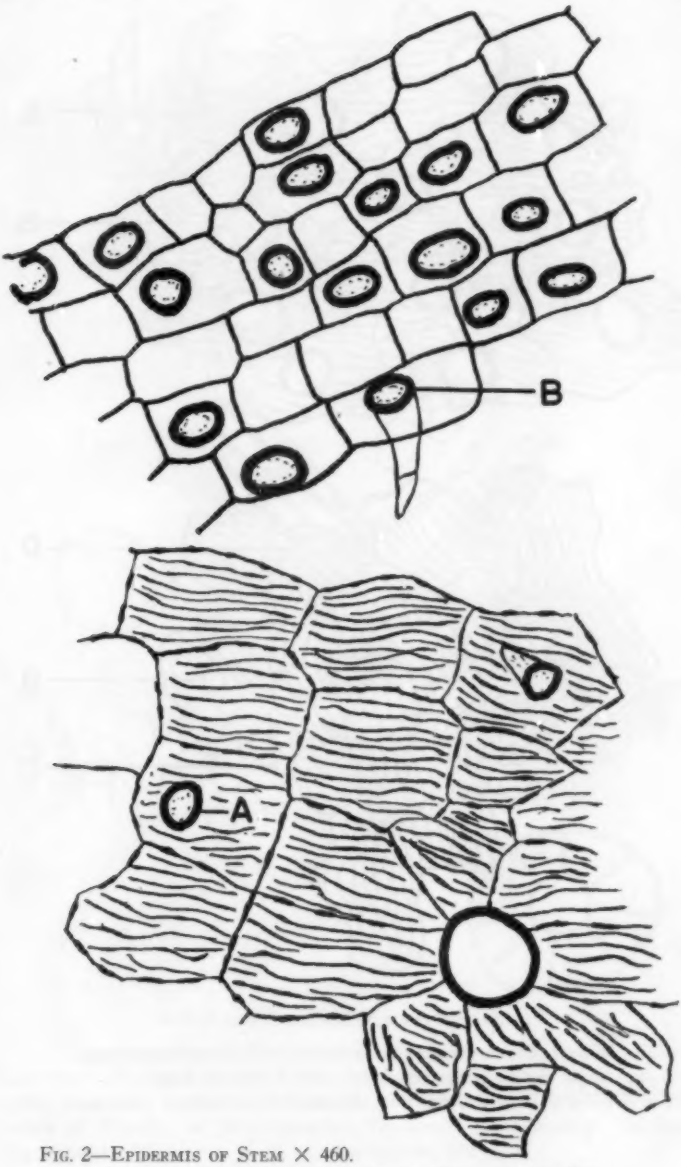


FIG. 2—EPIDERMIS OF STEM × 460.
(Top) Thymus Vulgaris. (Bottom) Thymus Serpyllum.
A—Trichome Scar. B—3-Celled, Non-Glandular Trichome.

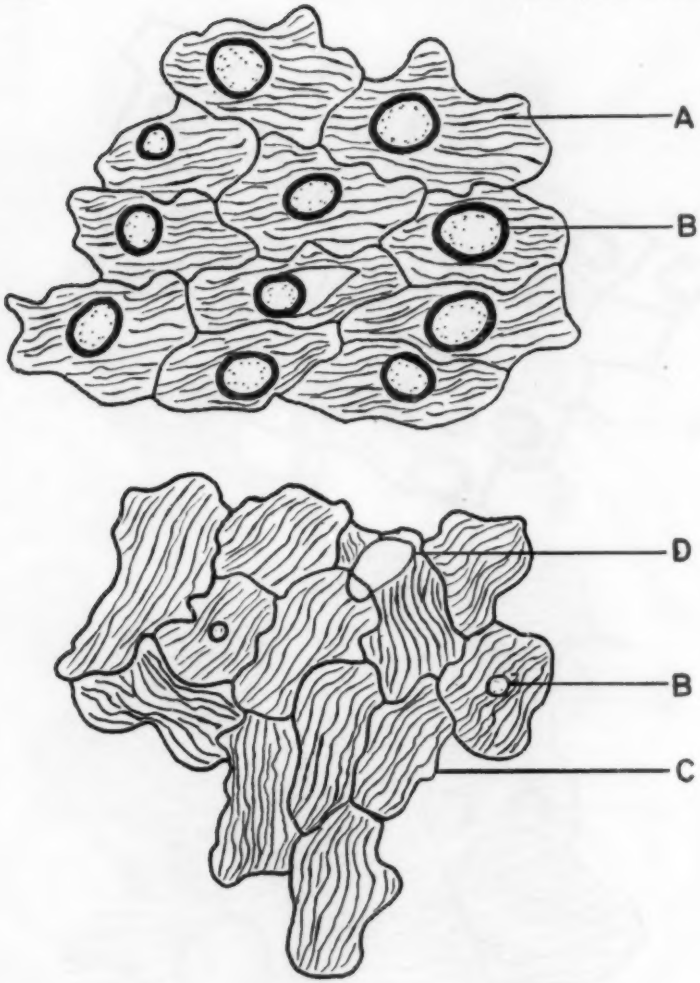


FIG. 3—EPIDERMIS OF CALYX TUBE × 410.

(Top) Thymus Vulgaris. (Bottom) Thymus Serpyllum.
A—Epidermal Striation. B—Trichome Scar.
C—Wavy Walled Epidermis. D—2-Celled Glandular Trichome.

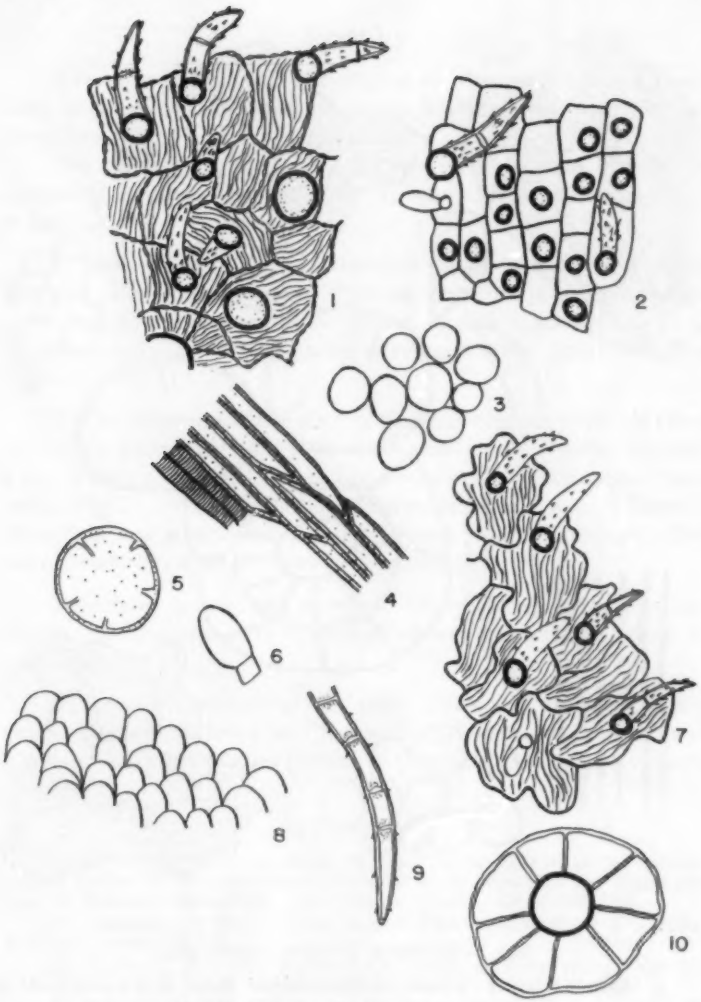


FIG. 4—POWDERED THYMUS VULGARIS.

1. Upper Epidermis of Leaf. 2. Epidermis of Stem. 3. Palisade Cells in End View. 4. Tracheae and Fibers from Vein. 5. Pollen Grain. 6. Two Celled Glandular Trichome. 7. Epidermis of Calyx Tube. 8. Papillose Epidermis of Corolla. 9. Non-Glandular Trichome. 10. Glandular Trichome. Magnification, #9 approx. 55 ×. Others approx. 250 ×.

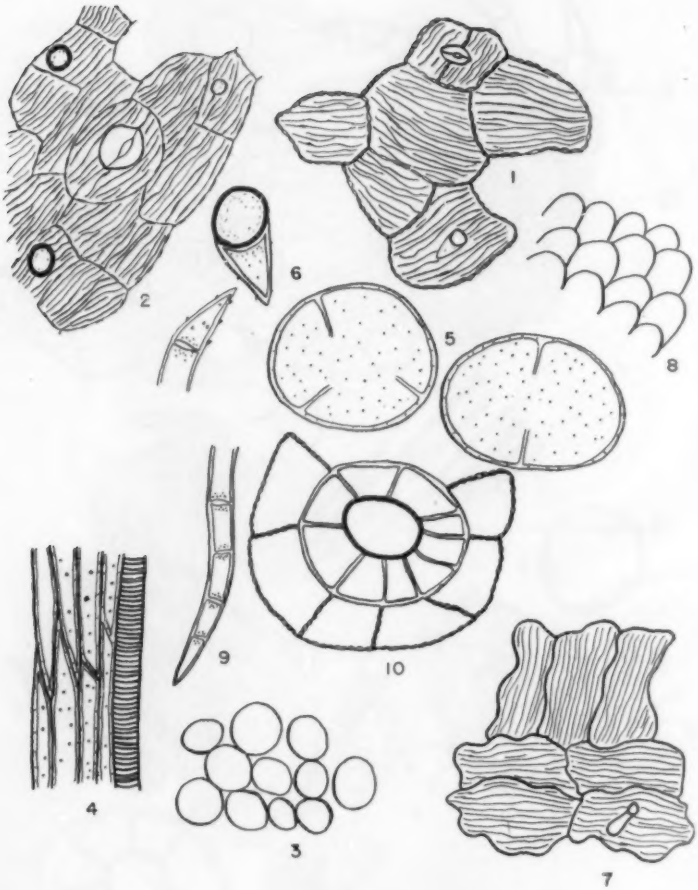


FIG. 5—POWDERED THYMUS SERPYLLUM.

1. Upper Epidermis of Leaf. 2. Epidermis of Stem. 3. Palisade Cells in End View. 4. Trachea and Fibers from Vein. 5. Pollen Grains. 6. Two Non-Glandular Hairs. 7. Epidermis of Calyx Tube. 8. Papillose Epidermis of Corolla. 9. Non-Glandular Trichome. 10. Glandular Hair With Neighboring Epidermal Cells. Magnification, #9 approx. 55 ×. Others 250 ×.

Summary

Although different samples studied of Thymus vulgaris showed little variation in degree of hairiness, it was found that Thymus Serpyllum samples varied considerably.

The outstanding histological features in the powder of value in separating Thymus vulgaris from Thymus Serpyllum were found to be:—

1. The leaf hair scars in abundance were present in Thymus vulgaris. This was not true of Thymus Serpyllum in which although scars were found they were not present in such numbers. Even in var. albus and var. coccineus, scars were much fewer than in Thymus vulgaris (Fig. 1).

2. The fragments of the stem of Thymus vulgaris when observed in surface view with epidermis uppermost either showed different kinds of nonglandular trichomes (as shown in table) attached or their scars (Fig. 2). Whereas the epidermal surface of the stem of Thymus Serpyllum rarely showed any such trichomes or scars although a few were present in var. albus and var. coccineus (Fig. 2).

3. Striated cuticle was found in Thymus Serpyllum stem epidermis, whereas the stem epidermis showed no striated cuticle in T. vulgaris.

4. The outer surface of the calyx when seen in surface view although almost glabrous in Thymus Serpyllum showed many nonglandular hairs or the scars formed by these hairs in Thymus vulgaris (Fig 3).

REFERENCES

(1) Silverman, H. I. and Dunn, M. S. The application of the palisade number method to the quantitative determination of spearmint and peppermint when in powdered admixtures. Am. Jour. of Pharm., 128:98-102, 1956.

(2) Youngken, H. W. A Text Book of Pharmacognosy, 6th Ed., Phila., Blakiston, 1948; 706-713.

(3) Bailey, L. H. The Standard Cyclopedia of Horticulture; Vol VI, New Edition; New York, The Macmillan Company, 1922; 3340-3342.

(4) Hegi, Gustav P. Illustrierte Flora Von Mittle Europa. Band V, Teil 4; Munchen; J. F. Lehmanns verlag; 2306-2327.

(5) Wittmack, L.; Garten Flora, Zeitschrift, Jahr gang 45; Berlin, 1896; 107-108.

(6) Grieve, M. A Modern Herbal, Vol. II; London; Jonathan Cape 30, Bedford Sq., 1931; 808-815.

(7) Rhode, E. S. Herb and Herb Gardening; New York, The Macmillan Company, 1937; 62-69.

DRUG INFORMATION SOURCES *

(India and Japan)

INDIA

The Indian Pharmaceutical Codex. Volume I. Indigenous Drugs Approved by the Pharmaceuticals and Drugs Research Committee, by B. Mukerji. New Delhi, Council of Scientific Research, 1953. 431 pp. Rs. 12.

A book of standards for indigenous drugs and preparations not included in the *British Pharmacopoeia* and the *Indian Pharmacopoeial List* (1947). Part I consists of monographs on natural products and drugs of vegetable and animal origin. These monographs are entered alphabetically under Latin or botanical name of drug and report synonyms, including common and local vernacular names, specifications, distribution and description in the case of plants, characteristics, constituents, actions, uses, tests and standards, assay, substitutes and adulterants, incompatibilities, storage and preparations employing the subject drug. Part II is a formulary of galenicals and other preparations of the drugs in Part I. An alphabetic index to common vernacular names and a general alphabetic index complete the volume. The Council's address is Old Mill Road, New Delhi. An office for the distribution of India Government publications is maintained at: Publications Division, Ministry of Information and Broadcasting, Government of India, New Delhi.

Materia Medica of Pharmaceutical Combinations and Specialties. 5th ed., by U. B. Narayanrao. Bombay, Medical Digest, 1954. LVII + 421 pp. Rs. 21-12.

Alphabetic list of specialties sold in India with brief information about manufacturer, composition, indications, dosage and forms. A comprehensive list of manufacturers with their Indian agents and addresses of both is included, as well as a therapeutic index to products listed. Publisher's address: Girgaum, Bombay 4.

---

* A World List; compiled by the Pharmaceutical Section, Science-Technology Division, Special Libraries Association.

Modern Pharmacology and Therapeutic Guide. 9th ed., by Rai Dr. A. R. Majumdar Bahadur. Calcutta, Scientific Publication Concern. 856 pp. Rs. 14.

According to advertising matter (1957), this guide is an up-to-date collection of drug information based on 500 selected prescriptions and more than 700 pharmaceutical preparations, indexed under 210 diseases. It incorporates *British Pharmacopoeia 1953* and *Addendum* 1955 and all new introductions of proven merit, as well as indigenous drugs, Indian food recipes and electrotherapy. Its author was professor of clinical medicine at the Medical College in Calcutta, now retired. Publisher's address: 9 Wellington Square, Calcutta 13.

India. Council of Scientific and Industrial Research. **The Wealth of India; A Dictionary of Indian Raw Materials and Industrial Products.** New Delhi, Dept. of Scientific Research, 1948 to date.

This encyclopedic compilation, rich in medicinal raw material information, has produced three volumes to date (A-B, 1948; C, 1950; D-E, 1952). It represents the contribution of the modern industrial and governmental scientist to the centuries-old wealth of India. The text comprises monographs on plant species under botanic names, metals, industrial products, building materials, etc. Entries are alphabetically arranged and report synonymous names, description, analysis, distribution, cultivation or production and uses, as well as citations to original literature. It is handsomely printed and illustrated. The Council's address is Old Mill Road, New Delhi.

Indian Materia Medica, by Dr. K. M. Nadkarni. 3d ed., revised and enlarged by A. K. Nadkarni. Bombay, Popular Book Depot, 1954. 2 Vols. (1319, 968 pp.) Approx. $18.00 for 2 volumes.

A compilation of information about Ayurvedic, Unani and home remedies. The whole of Volume 1 is devoted to Part I, The Vegetable Kingdom. Monographs are entered under botanic name of drug and include common vernacular names, habitat, parts used, constituents, actions, preparation and uses. There are 2671 entries in this

section, including cross references; many are comprehensive monographs. Part II covers the Mineral Kingdom (Ferri Sulphas, Hydrargyrum, Plumbum, Silicates, etc.) and Part III, Animal Kingdom. Separate pharmacologic and therapeutic indexes are included, as well as appendices listing Indian substitutes for foreign drugs, medicinal plants arranged by orders, chemical constituents of preparations in the three principal sections and supplementary information. List of additional references are appended to several of the sections. The general alphabetic index includes common names, but not botanical or other names used as titles of monographs. Publisher's address: Lamington Road, Bombay 7.

Indigenous Drugs of India; Their Medical and Economic Aspects, by R. N. Chopra. Calcutta, Art Press, 1933. 655 pp.

An old but comprehensive treatise on indigenous drugs, incorporating the results of laboratory chemical and pharmacological examination with traditional knowledge. The five parts of the book are described in the author's preface as follows: Part I, General considerations regarding the necessity of research into indigenous drugs; Part II, Economic considerations (i.e., descriptions, distribution, varieties, effect of storage) pertaining to pharmacopoeial and other drugs indigenous to India; Part III, chemical composition, pharmacologic action and therapeutic uses of drugs used in indigenous medicine; Part IV, A comprehensive list of Indian medicinal plants (over 2,000 plants) and short lists of drugs of animal and mineral origin; Part V, A short description of common bazar medicines of India, their important vernacular names and their popular uses. An alphabetic index to common vernacular names and a general alphabetic index complete the volume.

Medicinal Plants of India and Pakistan, by J. F. Dastur. Bombay, D. B. Taraporevala n.d. (1952?) 317 pp. Rs. 6.

This compilation is subtitled "A concise work describing plants used for drugs and remedies according to Ayurvedic, Unani, Tibbi systems and mentioned in British and American pharmacopoeias." It comprises 235 monographs; economic uses of some were previously described in the author's "Useful Plants of India and Pakistan."

Monographs are entered under botanical name of plant. Information about each includes Indian and English common names, description, distribution and a detailed discussion of uses. If description and distribution has previously been published in "Useful Plants", a cross reference to the earlier monograph is given and information is not repeated. Appendix I is a classification of plants according to their therapeutic uses. Publisher's address: 210, Hornby Road, Fort, Bombay 1.

JAPAN

Review of Clinical Drugs. Tokyo, Nippon Kajyoo Printing Co. Looseleaf. 3 Vols. (350-400 pp. each) 750 Yen; revision sheets, 450 Yen.

Comprehensive discussion of drugs and their actions, arranged in the following chapters: Vol. I, Fat-soluble vitamins; Water-soluble vitamins; Antibiotics; Drugs for allergic diseases; Anthelmintics. Vol. II, Drugs acting on digestive system; Drugs acting on central nervous system; Drugs affecting metabolism; Anti-tuberculosis drugs; Cardiovascular drugs. Vol. III, Drugs acting on urinary system; Hormones; Drugs acting on respiratory system; Drugs acting on sensory system; Drugs acting on autonomic system; Others. Composition, actions, indications and administration are treated in detail: A full description of disease states is given at the beginning of each chapter and literature references at the end. Individual chapters are written by different authors, usually professors at medical colleges. Additional looseleaf pages are sent every 3-5 months. Publisher's address: #2254 5-chome, Shiina-cho, Toshima-ku, Tokyo-to, Japan.

New Drugs. 8th ed. Tokyo, Pharmaceutical News Co., 1957. 244 pp. 300 Yen.

Text is classified broadly under the following headings: I, Recent topics; II, Anti-tumor drugs and antibiotics; III, Biochemical preparations (vitamins, etc.); IV, Pharmaceutical preparations (sedatives, diuretics, etc); V, Drugs used in public health (disinfectants, etc.). Information about individual drugs includes composition, actions and indications in detail, how administered, forms and prices, method of storing and manufacturer's name and address. Text is revised annually. Address of publisher: #43, 1-chome Jinbocho, Kanda-ku, Tokyo-to, Japan.

New Drugs in Common Use. 14th ed. Tokyo, Nihon Shinyaku Co., 1953. 381 pp. 350 Yen.

An alphabetic list of drugs, giving for each brief composition, indications and dosage and manufacturer's name and address. There are three sections: drugs for human use, veterinary drugs and an attached list of sulfa drugs and antihistamines. Publisher's address: 38-2, Mibu Shimomizo-machi, Nakagyo-ku, Kyoto.

Pharmaceutical Review. Card System of Pharmaceutical Review. Tokyo, Wako Shoin. May 1957 to date. Annual subscription, 860 Yen.

Cards are published for new drugs when they are put on the market; a new set is mailed every other month. Information supplied about individual drugs includes composition, action and indications in detail, side effects, precautions and contraindications, method of administration, manufacturer and address, forms and prices. Literature references are also cited. Cards may be arranged in alphabetic order or filed according to drug effects (as drugs acting on central nervous system, allergy drugs, drugs acting on the digestive system). Publisher's address: 1-29, Kampo-cho, Kanda, Chiyoda-ku, Tokyo.

Japan. Ministry of Welfare. **Formulae Nationales Japonicae.** 2d ed. Tokyo, Pharmaceutical News Co., 1950. 457 pp. 600 Yen. Supplement, 1957. 192 pp.

Monographs are arranged alphabetically by name of drug. Entries provide composition in detail, indicate dosage and describe methods of testing and preserving. Names in English are also included. Publisher's address: #43 1-chome Jinbocho, Kanda-ku, Tokyo-to, Japan.

Price List of Medical and Pharmaceutical Products. 5th ed. Tokyo, Pharmaceutical News Co., 1957. 320 pp. 350 Yen.

Drugs are listed in alphabetical order and individual entries give brief statement of actions and indications, manufacturer's name and forms and prices in detail. Price list is revised annually. Publisher's address, #43 1-chome Jinbocho, Kanda-ku, Tokyo-to, Japan.

The Committee on Drug Information Sources has the following members:

Anne McCann, Chairman; Elizabeth Boykin, Harold Oatfield, James L. Olsen, Jr., Maxine Painter, Elinor Piro, Clara Robeson, Walter Southern, Irene Strieby and Charlotte Studer.

A limited number of reprints are available for distribution by the Committee at 30¢ each. Requests should be sent to Miss Elinor Piro, Assistant Librarian, Winthrop Laboratories, 1450 Broadway, New York 18, N. Y.

Regular distribution will not be undertaken by the Section. Individuals and libraries wishing to ensure continued receipt of "Drug Information Sources" may do so by entering subscriptions to *American Journal of Pharmacy*.

Correspondence about "Drug Information Sources" should be directed to the Chairman at the Library, Squibb Institute for Medical Research, New Brunswick, N. J.

SELECTED ABSTRACTS

The Determination of Plasma Insulin and of Insulin Antagonists. Baird, C. W., and Bornstein, J. *The Lancet* No. 6979:1111 (1957). A method for extracting insulin from blood plasma was described by the authors. They showed that by fractionation insulin could be separated from its antagonists. The results of these studies revealed several interesting and valuable findings. Normal subjects, diabetics and insulin-resistant diabetics were included in the study.

The authors found that diabetics could be divided into two groups, those with and those without available insulin in their plasma. During diabetic coma, insulin was found to be present in the plasma but it was masked by an antagonist or antagonists. It was never found to be present as "free" insulin. These antagonists could be separated by the fractionation process used. However, there was some evidence to suggest that the extraction process employed caused the destruction of the antagonists present but in other instances did not. Therefore, it was felt that more than one antagonist may be present.

The authors speculated on the mechanism of action of the antagonist, whether the antagonist was binding the insulin in such a way that it was not available to the cell or whether it was acting upon some enzyme system. They also suggested that in healthy people there is a balance between insulin and its antagonists in the plasma but that this balance is upset when insulin resistance is present.

The Antifungal Activity of a Series of Parabens. Huppert, M. *Antibiot. and Chemother. 7:29* (1957). The antifungal activity of the parabens was compared with that of other compounds of known activity, including sorbic acid, tetramethylthiuram disulfide and caprylic acid. Caprylic acid was chosen by a preliminary study of the comparative activity against four strains of *Candida albicans* of a homologous series of fatty acids, from propionic acid to arachidic acid. A similar study was conducted using a homologous series of the esters of p-hydroxybenzoic acid. The hexyl and heptyl esters were the most active against *C. albicans*. Higher homologues were

almost completely inactive against this fungus. These more active parabens were then compared with caprylic acid, sorbic acid, and tetramethylthiuram disulfide in terms of the millimole concentration required to inhibit growth.

Hexyl- and heptylparaben proved to be more active against *C. albicans* than sorbic acid, tetramethylthiuram disulfide and caprylic acid. pH values from 6.0 to 7.5 had no effect upon the antifungal activity of the parabens. However, the three compounds used for comparison were less effective at neutral or slightly alkaline pH values. For example, the inhibitory concentration for hexyl- and heptylparabens at pH 7.5 was 0.1 mM but was more than 4.0 for the other three compounds.

Comparing the antifungal activity of caprylic acid with the two parabens against a series of 28 fungi commonly known to cause disease among humans, it was found that the parabens were superior or equal in every instance. It was also found that the parabens were not affected by the heat of sterilization in an autoclave.

The author suggested that hexylparaben and heptylparaben should be investigated for their antifungal activity in the treatment of fungus infections in man.

Inhibition of the Antibacterial Action of Tetracycline by Magnesium. Hamburger, M., Carleton, J., and Harcourt, M. *Antibiot. and Chemother. 7*:274 (1957). The antibacterial activity of oxytetracycline had been observed to have been reversed by certain divalent cations. The authors studied the effect of magnesium sulfate upon tetracycline in its action against several strains of staphylococci recovered from patients with septicemia. The organisms were strains of either *Staphylococcus aureus* or *S. albus*.

Chemically pure magnesium sulfate was dissolved in distilled water, at 10 times the concentration desired in the final mixture, and used for the making of agar plates. The organism and the desired quantity of tetracycline was introduced and the plates incubated at 37° C. The authors compared the number of colonies of one strain of *S. aureus* that developed on plates containing no tetracycline and 1, 2, 3, or 5 micrograms per ml. against concentrations of magnesium sulfate varying from 0 to 100,000 micrograms per ml. It was found that 3000 micrograms per ml. of magnesium sulfate could almost completely inhibit the action of 1 microgram per ml. of tetracycline. To

inhibit 5 micrograms per ml. of tetracycline, 50,000 micrograms of magnesium sulfate were required. In terms of molecular weight the authors concluded that 3500 to 6000 parts of magnesium sulfate are required to inhibit 1 part of tetracycline. In addition to a reduction in number of colonies which developed where a less than complete inhibiting quantity of magnesium sulfate was present, the colonies were usually smaller than normal.

The authors illustrated the value of magnesium in unmasking falsely negative cultural findings because of the carrying over of minimal inhibiting quantities of tetracycline into subcultures. The study here reported developed from the need of a method for inhibiting small quantities of tetracycline carried over into culture studies from the blood of patients receiving the antibiotic.

The Treatment of Pediatric Infections with Sulfisoxazole. Carter, C. H., and Maley, M. C. *Med. Times 85:762* (1957). The development of the tasteless acetyl derivative of sulfisoxazole has greately facilitated the oral use of this antibacterial agent in children. Recent findings that absorption of this compound is improved, giving higher and more prolonged blood levels, from a fat emulsion has further increased its usefulness.

The authors reported a study in which acetyl sulfisoxazole was administered orally as a vegetable oil emulsion containing 20 per cent of the drug. This was equivalent to 1 Gm. per teaspoonful. The usual dosage was about 100 mg. per day per pound body weight in two to three divided doses. A total of 142 children with a variety of common bacterial infections were treated. Bacteriological studies including cultures and sensitivity tests were performed in most cases.

Of the 142 cases treated, 132 showed a clinical cure within six days. Forty six of these responded within 3 days. Only two patients were classified as not cured. One patient with purulent otitis media still had drainage after 16 days and one patient with bronchopneumonia due to *Proteus morganii* failed to respond.

A summary of the organisms cultured was tabulated by the authors. *Staphylococcus aureus* showed the highest incidence. It was found alone in 22 cases and with other organisms in 25 cases. The sensitivity of the organisms against acetyl sulfisoxazole and various

antibiotics was determined. There was no significant correlation between the sensitivity determination and the clinical response to therapy with acetyl sulfisoxazole.

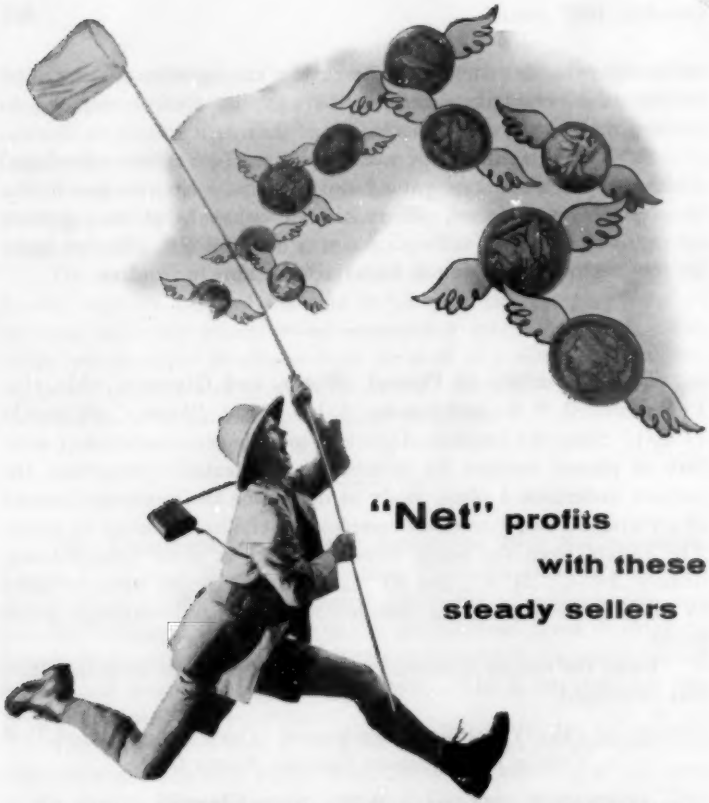
Side effects from therapy were minimal. Two patients developed a skin eruption and one patient an urticaria. No changes in the blood picture were found. The authors concluded that the vegetable oil emulsion of acetyl sulfisoxazole was a useful and effective agent for the treatment of common bacterial infections in children.

The Miscibility of Phenol, Water, and Glycerin. Matyba, E. R., Connell, P. E., and Murray, J. P. *Canad. Pharm. J. 90*:66-438 (1957). Since the addition of glycerin to an aqueous solution or mixture of phenol reduces its disinfectant and caustic properties, the authors undertook a phase study to determine the minimum amount of glycerin necessary to effect complete miscibility of phenol in water. The results from the study were tabulated at three temperatures, namely, 18° C., 24° C., and 30° C. Phase diagrams were prepared by plotting the percentages obtained on triangular co-ordinate graph paper.

From the results obtained the following practical table of values was developed.

Percentage (W/W) of Each Component Which When Mixed Will Yield a Homogeneous Solution Above 60° F.

Phenol	Water	Glycerin
10	75	15
15	67	18
20	61	19
25	57	18
30	52	18
35	48	17
40	44	16
45	40	15
50	37	13
55	34	11
60	31	9
65	29	6
70	27	3



"Net" profits with these steady sellers

S. T. 37® — Essentially non-toxic, multiple-use antiseptic. Harmless even if swallowed.

SUCRETS® — A soothing lozenge for speedy throat relief.

TYROLARIS® — The first antibiotic mouthwash. Cleans, refreshes.

TRACINETS® — Antibiotic troches with local anesthetic action.

MSD

MERCK SHARP & DOHME

DIVISION OF MERCK & CO., INC., PHILADELPHIA 1, PA.

GOOD MEDICINE FOR MORE SALES

MYADEC®

capsules

Increasingly, doctors are selecting MYADEC Capsules for their nutritionally deficient patients because of the dependable, comprehensive aid they provide—9 important vitamins in therapeutic potencies together with 11 valuable minerals and trace elements. Patients like MYADEC, too, because it's easy to take (only one capsule a day) and economical as well. As a result of this increasing doctor-patient preference, MYADEC is good medicine for stepping up sales Is your supply adequate?

MYADEC Capsules are supplied in bottles of 30, 100, and 1,000.

PARKE, DAVIS & COMPANY **DETROIT 32, MICHIGAN**

Expanding Meti-steroid benefits to an ever-broadening field of therapy

METICORTEN® Tablets

METICORTELONE® Tablets

METICORTELONE Acetate Aqueous Suspension

SIGMAGEN* Tablets

METI-DERM* Cream

METI-DERM Ointment with Neomycin

METIMYD* Ophthalmic Suspension

METIMYD Ointment with Neomycin

METRETON* Tablets

METRETON Nasal Spray

Schering

*TM

American Journal of Pharmacy

The American Journal of Pharmacy is the oldest continuously published scientific periodical of its kind in America, having been established by the Philadelphia College of Pharmacy in 1825. After the original issue there were three other preliminary numbers until 1829, when regular publication began. From then until 1852 four issues were published annually, with the single exception of 1847, when an additional number appeared. Six issues a year were printed from 1853 to 1870, at which time the Journal became a monthly publication.

Former Editors of the Journal have been: Daniel B. Smith, 1825-1828; Benjamin Ellis, 1829-1831; Robert E. Griffith, 1831-1836; Joseph Carson, 1836-1850; William Procter, Jr., 1850-1871; John M. Maisch, 1871-1893; Henry Trimble, 1893-1898; Henry Kraemer, 1898-1917; George M. Beringer, 1917-1921, and Ivor Griffith, 1921-1941.

Established and maintained as a record of the progress of pharmacy and the allied sciences, the Journal's contents and policies are governed by an Editor and a Committee on Publications elected by the members of the College.

Manuscripts should be sent to the Editor, who does not assume any responsibility in connection with the views or investigations of contributors of accepted manuscripts, other than to exercise general care in selection.

Contributors are allowed a reasonable number of copies of this Journal, free of charge, if applied for when the proof is returned.

Reprints, if desired, should be ordered when the proof is returned. The table below shows the *approximate* cost of reprints, the make-up of the pages to be identically the same as in the Journal. The actual cost may vary from the figures given, and will depend upon the amount of presswork, paper, binding, and other factors. Reprints containing half-tones may be expected to cost somewhat more than the rates given.

	2 pp.	4 pp.	8 pp.	16 pp.	Covers with Titles	
50 copies.....	$ 4.50	$10.00	$16.25	$27.50	50 copies.....	$ 7.50
100 "	7.50	13.75	21.25	40.00	100 "	12.50
250 "	10.00	17.50	27.50	53.75	250 "	17.50
500 "	15.00	25.00	35.00	68.75	500 "	26.25

Everybody benefits
when everybody gives